

PATENT COOPERATION TREATY

AG

From the INTERNATIONAL SEARCHING AUTHORITY *Loh*

PCT

To:
HADASSA WATERMAN
G.E. EHRLICH (1995) LTD.
11 MENACHEM BEGIN STREET
RAMAT GAN, ISRAEL 52521

RECEIVED

26 AUG 2008

FILE No. 32000

G.E. EHRLICH (1995) LTD.

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year) 14 AUG 2008 d

Applicant's or agent's file reference
32000

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/IL06/00795

International filing date
(day/month/year) 09 July 2006 (09.07.2006)

Applicant
FULCRUM SP LTD.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☒ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☒ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer:

Kathleen Kerr Bragdon
Kathleen Kerr Bragdon/

Telephone No. 571-272-1600

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 32000	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/IL06/00795	International filing date (<i>day/month/year</i>) 09 July 2006 (09.07.2006)	(Earliest) Priority Date (<i>day/month/year</i>) 07 July 2005 (07.07.2005)
Applicant FULCRUM SP LTD.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☐

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of:

☒

the international application in the language in which it was filed.

☐

a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐

This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 Rule 43.6 *bis(a)*

c. ☒

With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐

Certain claims were found unsearchable (See Box No. II)

3. ☒

Unity of invention is lacking (See Box No. III)

4. ☒

With regard to the **title**,

☒

the text is approved as submitted by the applicant.

☐

the text has been established by this Authority to read as follows:

5. ☒

With regard to the **abstract**,

☒

the text is approved as submitted by the applicant.

☐

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. ☒

With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐

as suggested by the applicant.

☐

as selected by this Authority, because the applicant failed to suggest a figure.

☐

as selected by this Authority, because this figure better characterizes the invention.

b. ☒

none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL06/00795

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item I.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



on paper



in electronic form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL06/00795

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1,2,5-11,19-25 and 28-41 (SEQ ID NO: 2 and 3)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL06/00795

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07K 1/00(2006.01);C07H 21/02(2006.01);C12Q 1/64(2006.01)

USPC: 530/350;536/23.1;435/9

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350; 536/23.1; 435/9

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubMed, WEST, STN

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WANG et al. Characterization of SPI, a Stress-Responsive, Boiling-Soluble, Homo-Oligomeric Proteic from Aspen. Plant Physiology. 2002, Volume 130, pages 865-875, entire document.	1, 5-9, 19-22, 28-31 and 39-41
A	PELAH et al. Characterization of BspA, a major boiling-stable, water-stress-responsive protein in aspen (Populus tremula). Tree Physiology. 1995, volume 15, pages 673-678.	1-2, 5-11, 19-25 and 28-41
A	DGANY et al. The Structural Basis of the Thermostability of SPI, a Novel Plant (Populus tremula) Boiling Stable Protein. Journal Biological Chemistry. 03 December 2004, Volume 279, pages 51516-51523.	1-2, 5-11, 19-25 and 28-41



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

06 June 2008 (06.06.2008)

Date of mailing of the international search report

14 AUG 2008

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Kathleen Kerr Bragdon

Telephone No. 571-272-1600

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-2, 5-11, 19-25 and 28-41, drawn to an isolated polypeptide comprising an amino acid sequence of an SP1 polypeptide, said amino acid sequence being modified to be in a reversible molecular association with a substance, relating to the polypeptide of SEQ ID NO: 2.

Groups 2, 3, 4 -- 29, claim(s) 1-2, 5-11, 19-25 and 28-41, drawn to an isolated polypeptide comprising an amino acid sequence of an SP1 polypeptide, said amino acid sequence being modified to be in a reversible molecular association with a substance, relating to the polypeptide of SEQ ID NO: 3, 4, 5 -- 30, respectively.

Groups 30, 31, 32 -- 58, claim(s) 3-4, drawn to an isolated polynucleotide of Claim 1 including the nucleic acid comprising a nucleic acid sequence encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO: 2, 3, 4 -- 30, respectively.

Groups 59, claim(s) 12-13, 19-27, 32-34 and 36-37, drawn to a method of delivering a therapeutic, diagnostic or cosmetic agent to a subject in need thereof, the method comprising administering effective amount of the composition of matter of any of claims 6 or 7.

Groups 60, claim(s) 14-28, 30, 32-37, drawn to a method of stabilizing a substance or enhancing the solubility of a substance in a solution, the method comprising contacting the substance with a modified SP1 polypeptide and/or contacting a solvent.

The inventions listed as Groups 1-60 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions are linked by the technical feature of an isolated modified polypeptide comprising an amino acid sequence of an SP1 polypeptide to be in a reversible molecular association with a substance. However, this technical feature is not special because it does not constitute an advance over the prior art by Zhang et al. (1998, The Journal of Biological Chemistry, vol. 273, pages 12281-12287). Zhang et al. disclose an isolated active site mutant of protein tyrosine phosphatases (i.e., PTPase with D181A mutation) as evidenced by the kinetic parameters of PTPase shown in Table 1, page 12283. The mutant PTPase by Zhang et al. was stable enough to be used in the kinetic study; thus, it is encompassed by the instant SP1, which is "referred to herein as stable protein (see top of instant specification page 1). The PTPase of Zhang et al. also have sequence modification and have shown a reversible binding with a substance Suramin (see top of left column, page 12283). Thus, the mutant PTPase of Zhang et al. meets all limitations of Claim 1, which is SP1 with modified amino acid sequence and having reversible molecular association with a substance. The invention of Group 1, a first product, requires as its technical feature of modified SP1 and relating to SEQ ID NO: 2. This technical feature is not required by Groups 2-58 by virtue of distinct structure having distinct sequence. Groups of 59-60 are method compared to the product of Group 1. Thus, the Groups 1-60 lack the unity of invention because the invention of Group 1, a first product, requires as its technical feature, wherein the technical feature is not special. Thus, Groups I-IV do not relate to a single general inventive concept.